REMARKS

FORMAL MATTERS:

Claims 10-41 are pending. Claims 10, 17-20, 25, 26, 32, and 34-37 have been amended to correct antecedent basis for certain dependent claims. Support for the changes appears, for example, in dependent claims 21 and 38. No new matter has been added.

OBJECTION TO THE DRAWINGS

The Examiner has objected to the drawings under 37 C.F.R. § 1.83(a) for failing to show protein levels as described in the specification.

At paragraph [0017] of the specification, in the BRIEF DESCRIPTION OF THE DRAWINGS, Applicant discloses determining protein levels by Western blot analysis. Figure 1B is a Western blot. One skilled in the art at the time of Applicant's filing date would have known how to determine protein levels from a Western blot. Paragraph [0017] discloses determining protein levels and not the actual determined levels of proteins. Therefore, Applicant submits that a figure showing protein levels is not essential for a proper understanding of the disclosed invention.

Applicant respectfully requests reconsideration and withdrawal of this objection.

REJECTIONS UNDER 35 U.S.C. § 112, ¶1

Enablement Requirement

Claims 18-20 and 35-37 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. This rejection is respectfully traversed.

The Examiner has asserted that one cannot practice the claimed invention without the cell lines recited in the rejected claims, and that the cell lines must be known or readily available to the public, obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public.

All of the cell lines recited in the rejection (MRC-5, WI-38, Chang liver, U937, MRC-9, IMR-90, IMR-91, Lederle 130, CEM, and CD4-expressing HUT78) are in fact commercially and readily available. All but IMR-91 and Lederle 130 are available from the American Type Culture Collection and are listed in their catalog that is searchable online. The cell lines IMR-91 and Lederle 130 are

commercially available from the NIA Cell Repository of the Coriell Institute for Medical Research, Camden, NJ, and are listed in their catalog that is searchable online. Applicant is willing to amend the specification to include this information if the Examiner so desires.

Withdrawal of this rejection is respectfully requested.

Claims 10-41 were also rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement ("how to make") requirement. This rejection is respectfully traversed.

The Examiner asserted that the specification fails to mention where to make the deletion in the three genes claimed, and that one of skill in the art would not have known where to introduce the deletion such that the resulting cell has increased permissiveness to viral replication owing to the deletion. Further, she asserted that "[t]here is no structure/function correlation and no method of making the claimed product. Office Action at page 6.

Initially, Applicant notes that it would appear that an argument regarding structure/function correlation is not germane to a *how to make* enablement rejection. Clarification is requested.

When rejecting a claim under the enablement requirement of section 112, the Examiner bears the "initial burden of setting forth a reasonable explanation as to why [he/she] believes that the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner bears the burden of providing **evidence or technical reasoning** to substantiate her doubts that the specification is not enabling with respect to the scope of a claim sought to be patented. *Ibid. See also* MPEP § 2164.04. Without evidence or technical reasoning to doubt the truth of the statements made in the application, the application must be considered enabling. *Ibid.* In addition, an enablement rejection should be stated with a full development of the reasons rather than by a mere conclusion coupled with some stereotyped expression. MPEP § 706.03.

The proper standard for establishing enablement is one of undue experimentation, i.e., is the experimentation needed to practice the invention undue or unreasonable? See MPEP § 2164 entitled Test of Enablement. The undue experimentation standard for enablement was elucidated in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) via a list of eight factors to be considered. These factors are (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples relating to the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability

of the art; and (8) the breadth of the claims. The Examiner has not employed an undue experimentation analysis in her rejection. Moreover, the Examiner's conclusions appear to be doubts unsubstantiated by evidence or technical reasoning, and appear to be mere conclusions coupled with stereotyped expression, specifically proscribed by MPEP § 706.03.

Applicant submits that undue experimentation would not be required to make the claimed invention. The claims recite targeted deletions in three genes, each of which is known. The nature of the invention is the preparation of gene knock-outs, which is a well-established field, and techniques for making the gene knock-outs in known genes are well-known in the art. Guidance to the relevant literature for making the gene knock-outs is disclosed in the specification. The art is not unpredictable, i.e., one would know when a product has been made. The skill of the routineer in this art is high, so that the syntheses would be considered routine, especially in light of the body of published literature on the subject. Working example 5, beginning at page 20, discloses how to assay cells for increased permissiveness to viral replication. Accordingly, the quantity of experimentation would not be undue, because by performing a routine assay after performing a routine synthesis, one may make an invention within Applicant's claims. Enablement is not precluded by the necessity for some experimentation, such as performing routine assays. In fact, a considerable amount of experimentation is permissible if the experimentation is merely routine, or if, as here, the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should take. *Ex parte Jackson*, 217 USPQ 804, 807 (Bd. App. 1982).

Furthermore, the specification need not disclose what is well-known to those skilled in the art, and preferably omits that which is well-known to those skilled and already available to the public. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Applicant's specification at paragraph [0023] discloses that targeted gene deletion ("gene knock-out") is a technique that is well-known in the art for making PKR-deficient cells, and cites two exemplary references. At paragraphs [0031] and [0033] Applicant discloses that cell cultures deficient in 2'-5'oligoadenylate synthetase activity and deficient in MxA protein activity, respectively, can be isolated in a fashion similar to that used for cell cultures deficient in PKR. Therefore, pursuant to *Hybritech*, there is no need to disclose this well-known technique in Applicant's specification.

Withdrawal of this rejection is respectfully requested.

Written Description Requirement

Claims 10-41 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

The Examiner asserted that "[t]he actual deletion is not recited in the claims, nor is it clear from the specification where to make the deletion in each of the three genes claimed such that the cell has increased permissiveness to viral replication." Office Action at page 3.

Two recent court decisions make it clear that a determination of what is needed to describe generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. *See Capon v. Eshar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). Further, in *Bilstad v. Wakalopulos,* 386 F.3d 1116 (Fed. Cir. 2004), the court remanded the case to the Board because the record contained no analysis of what skilled in the art would have understood from the disclosure or the degree of predictability of technical variations in this field of art. *Bilstad* at 1126.

The Examiner will note from these cases that a proper analysis for written description is not unlike the *Wands* analysis that is required for undue experimentation in an enablement context. Therefore, Applicant reiterates his arguments above with respect to the *Wands* factors to the extent they apply to written description. Because there is no analysis on this record regarding why the description is beyond scientific capability, the rejection is improper. Further, both *Capon* and *Bilstad* relate to the written description required for generic inventions. Applicant submits that an even lower standard should be used when, as here, only three genes and not a large genus are recited.

Finally, the court has held recently that the written description requirement and enablement requirements "usually rise and fall together. That is a recitation of how to make and use the invention across the full breadth of the claim is ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice versa." *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005).

Withdrawal of this rejection is respectfully requested.

DOUBLE PATENTING REJECTIONS

Claims 10-41 were rejected for nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent No. 6,673,591.

Accordingly, filed herewith is the requisite terminal disclaimer in view of which Applicant respectfully requests that this rejection be withdrawn.

Claims 10-41 were rejected for nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of US Patent No. 5,840,565.

Accordingly, filed herewith is the requisite terminal disclaimer in view of which Applicant respectfully requests that this rejection be withdrawn.

Claims 10-41 were rejected for nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of US Patent No. 6,686,190.

Accordingly, filed herewith is the requisite terminal disclaimer in view of which Applicant respectfully requests that this rejection be withdrawn.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSF-285CON5.

Respectfully submitted,
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Enclosure(s): Terminal Disclaimers (3)

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